**SUMMARY**

Examples herein include but are not limited to methods, devices, compositions, kits, materials, tools, instruments, reagents, products, compounds, pharmaceuticals, arrays, computer-implemented algorithms, and computer-implemented methods.

In one aspect, there is provided a method of producing an implantable collagen-containing medical device comprising the step of coating said collagen-containing medical device with metal microparticles and/or metal nanoparticles, wherein said step of coating said collagen-containing medical device is by sonication such that the collagen-containing medical device has anti-bacterial and anti-inflammatory properties on implantation compared to the medical device not coated with metal microparticles and/or metal nanoparticles.

In another aspect, the present disclosure provides a method for inhibiting biofilm formation on a medical implant, comprising the step of covering said implant with a collagen-containing membrane that has been coated with silver nanoparticles so as to prevent biofilm formation and/or growth of bacteria.

In yet another aspect, the present disclosure provides a method for inhibiting microbial colonization on a medical device or implant, comprising covering said device or implant with a collagen-containing membrane that has been coated with silver nanoparticles so as to prevent microbial colonization.

In yet another aspect, the present disclosure provides a package comprising a collagen-containing medical device that is coated with silver nanoparticles, wherein said silver nanoparticles have been applied by sonication, wherein said device is sealed in an airtight or vacuum-packed container.

In one example, the medical device can be delivered into a host organism, such as a human or animal, or used *in vitro*. The medical device may comprise plasmids, genes, nucleic acids, or a DNA or RNA virus.

In another example, the coating covers at least a portion of said device. The metal micro and/or nanoparticle coating can further comprise natural or synthetic polymers, metal, metal oxide, oxide, metal nitride, borate, ceramic, zirconia, allograft hard tissue, allograft soft tissue, xenograft hard tissue, xenograft soft tissue, carbon nanostructure, carbon, glasses, natural, or biocompatible material. The coating is capable of performing at least one of treating infection, preventing infection; promoting cell adhesion; preventing biofilm formation, inhibiting biofilm formation; promoting cell proliferation; promoting binding with a biological or non-biological system, increasing or decreasing a cell function; delivering a drug and/or bioactive agent, or ensuring a better integration of a material into the host tissue.

In other examples, the coating comprises one or more layers of nanoparticles and/or microparticles. In still other examples, the one or more layers comprises a single type of nanoparticle and/or microparticle, or a combination of more than one type of nanoparticle and/or microparticle. Further, one or more layers comprises silver nanoparticles. In another example, one or more layers comprises a combination of metal, nanoparticles, metal oxides, carbon nanotubes, polymeric nanoparticles, ceramics, calcium phosphate, collagen, and/or hydroxyapatite nanoparticles. In other examples, the coating is biodegradable and/or biocompatible, and nanoparticles can be released from said nanoparticle composition as each layer degrades. In other

examples, a drug, growth factor, and/or bioactive agent is deposited within at least one layer and/or on the surface layer of said coating. In other examples, the nanoparticles comprise gold, silver, metals, oxides, carbon nanostructures (single, double, multi walled nanotubes, graphenes, fullerenes, nanofibers), hydroxyapatite, zirconia, natural or synthetic polymers, ceramics, or metal oxide.

In other examples, the medical device is an orthopaedic implant, dental implant, veterinary prosthetic device, tissue engineering matrix, allograft hard tissue or allograft soft tissue. The orthopaedic implant is a hip implant, knee implant, shoulder implant, plate, pin, screw, wire, or rod. The dental implant is an abutment, healing screw, or cover screw. The veterinary prosthetic device is an implant, pin, screw, plate, or rod.

In other examples, the coating comprises one or more layers comprise at least one of a protein, amino acid, enzyme, nucleic acid, bioactive agent, growth factor, drug, antibiotic, nucleic acid, hormone, antibody, or agent that inhibits biofilm formation and may be released as layer(s) degrade. In a further example, the growth factor is a bone morphogenic protein capable of promoting bone formation adjacent to or on the surface of a device. In another example, the bioactive agent is in or on the surface coating of a medical device and affects adjacent tissue or cells in at least one or more of bone formation, protein synthesis, gene, expression, cell proliferation, mitosis, DNA transcription, hormone production, enzyme production, cell death, gene delivery, or drug delivery. In a still further example, the bioactive agent may be linked to said nanoparticles and the linkage may be a covalent, ionic, hydrogen bond, sulfide bond, or polar covalent bond.

In another example, there is provided a method for inhibiting biofilm formation on a collagen-containing medical implant, comprising the step of coating said medical implant with metal microparticles and/or nanoparticles by sonication such that the medical implant on implantation has anti-bacterial and anti-inflammatory properties compared to the medical implant not coated with metal microparticles and/or nanoparticles by sonication.

Also provided is a collagen-containing medical implant coated with metal microparticles and/or nanoparticles by sonication for use in a method for inhibiting biofilm formation on the medical implant, wherein the medical implant on implantation has anti-bacterial and anti-inflammatory properties compared to the medical implant not coated with metal microparticles and/or nanoparticles by sonication.

In one example, a biofilm is a bacterial, fungal, or protozoan biofilm. In another example, a medical implant is an orthopaedic or dental implant, graft, bone material, scaffold, allograft hard tissue, allograft soft tissue or tissue engineering matrix.

In another example, there is provided a method for inhibiting microbial colonization on a collagen-containing medical device or implant, comprising coating said device or implant with metal microparticles and/or metal nanoparticles by sonication that prevents microbial colonization.

Also provided is a collagen-containing medical device or implant coated with metal microparticles and/or nanoparticles by sonication for use in a method for inhibiting microbial colonization on the device or implant, wherein the metal microparticles and/or nanoparticles prevent microbial colonization.

In one example, the collagen-containing device or implant is a dental implant, orthopaedic implant, veterinary implant, scaffold or tissue engineering matrix.

In another example, there is a collagen-containing implant comprising silver nanoparticles, wherein said silver nanoparticles coat at least one surface of said implant. In one example, the implant is a dental implant or an abutment for a dental implant.

In another example, there is provided a method of sterilizing a collagen-containing metal nanoparticle-coated medical device, comprising exposing said device to either ethylene oxide or gamma radiation.

In another example, there is provided a package comprising a collagen-containing metal nanoparticle-coated medical device, wherein said device is sealed in an airtight or vacuum packed container. In one example, the medical device is a dental implant, an abutment for a dental implant, or any medical device.

In another example, there is provided a method for enhancing bone cell growth, comprising (a) depositing metal nanoparticles on a surface of a collagen-containing membrane to create a surface coating; and (b) culturing osteoblasts on said surface.

**CLAIMS**

1. A method of producing an implantable collagen-containing medical device comprising the step of coating said collagen-containing medical device with metal microparticles and/or metal nanoparticles, wherein said step of coating said collagen-containing medical device is by sonication such that the collagen-containing medical device has anti-bacterial and anti-inflammatory properties on implantation compared to the medical device not coated with metal microparticles and/or metal nanoparticles.

2. A method according to claim 1, wherein the metal microparticles and/or metal nanoparticles comprise a metal selected from the group consisting of silver and copper or combinations thereof.

3. A method according to claim 1, wherein the collagen-containing medical device is a collagen-containing membrane.

4. A method according to claim 1, wherein the collagen-containing medical device is for delivery into a host organism or used *in vitro*.

5. A method according to claim 4, wherein the host organism is a human or animal.

6. A method according to claim 1, wherein the coating covers at least a portion of said device.

7. A method according to claim 1, wherein the coating further comprises natural or synthetic polymer, metal, metal oxide, oxide, metal nitride, borate, ceramic, zirconia, allograft hard tissue, allograft soft tissue, xenograft hard tissue, xenograft soft tissue, carbon nanostructure, carbon, glasses, natural or biocompatible material.

8. A method according to claim 1, wherein the metal microparticles and/or metal nanoparticles have a size range from about 0.5 nm to about 500 nm.

9. A method according to claim 1, wherein the coating is capable of performing at least one of: treating infection; preventing infection; treating inflammation; preventing inflammation; promoting cell adhesion; preventing biofilm formation; inhibiting biofilm formation; promoting cell proliferation; promoting binding with a biological or non-

biological system; increasing or decreasing a cell function; delivering a drug and/or bioactive agent, or ensuring a better integration of a material into the host tissue.

10. A method according to claim 1, wherein the coating comprises metal microparticles and metal nanoparticles.

11. A method according to claim 1, wherein the coating comprises metal nanoparticles.

12. A method according to claim 1, wherein the coating comprises one or more layers of metal nanoparticles and/or metal microparticles.

13. A method according to claim 12, wherein the one or more layers comprises silver nanoparticles.

14. A method according to claim 1, wherein the medical device is an orthopaedic implant, dental implant, veterinary prosthetic device, a scaffold or a tissue engineering matrix.

15. A method according to claim 14, wherein the orthopaedic implant is a hip implant, knee implant or shoulder implant.

16. A method according to claim 14, wherein the dental implant is an abutment.

17. A method for inhibiting biofilm formation on a medical implant, comprising the step of covering said implant with a collagen-containing membrane that has been coated with silver nanoparticles so as to prevent biofilm formation and/or growth of bacteria.

18. A method according to claim 17, wherein the biofilm is a bacterial, a fungal, or a protozoan biofilm.

19. A method according to claim 17, wherein the medical implant is an orthopaedic or a dental implant, a scaffold or a tissue engineering matrix.

20. A method for inhibiting microbial colonization on a medical device or implant, comprising covering said device or implant with a collagen-containing membrane that has been coated with silver nanoparticles so as to prevent microbial colonization.

21. A package comprising a collagen-containing medical device that is coated with silver nanoparticles, wherein said silver nanoparticles have been applied by sonication, wherein said device is sealed in an airtight or vacuum-packed container.